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Detection of people at risk of developing a first psychosis: comparison of two recruitment strategies

Rietdijk J, Klaassen R, Ising H, Dragt S, Nieman DH, van de Kamp J, Cuijpers P, Linszen D, van der Gaag M. Detection of people at risk of developing a first psychosis: comparison of two recruitment strategies.

Objective: Better recruitment strategies are needed to improve the identification of people at ultra-high risk of developing psychosis. This study explores the effectiveness of two recruitment strategies: a screening method in a consecutive help-seeking population entering secondary mental health services for non-psychotic problems vs. a population referred to the diagnostic center of an early-psychosis clinic.
Method: From February 2008 to February 2010, all general practitioner and self-referrals (aged 18–35 years) to the secondary mental healthcare service in The Hague and Zoetermeer were screened with the Prodromal Questionnaire; patients who scored above the cutoff of 18 and had a decline in social functioning were assessed using the Comprehensive Assessment of At-Risk Mental States (CAARMS). All referrals (aged 14–35 years) to the diagnostic center in Amsterdam were also assessed with the CAARMS.
Results: The screening detected a three-fold higher prevalence of at-risk mental states: these subjects were older and more often female. MANOVA showed significantly higher scores for the screened population on depression, social anxiety, distress with positive symptoms, and a higher rate of transition to psychosis within 12 months.
Conclusion: The screening method detects more patients with at-risk mental states than the referral method. The latter method is biased to young male patients in an earlier prodromal stage and a lower transition rate.

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Key words: early detection; at-risk mental states; ultra-high-risk screening; psychosis

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Significant outcomes

- Screening detected more patients with at-risk mental states or psychosis at the gate of the mental health services than did referral.
- Screening did not lead to an increase in the number of false-positive cases, as demonstrated by the higher transition rates in the screened population compared to the referred population.
- In the at-risk mental state stage, both sexes showed similar subclinical psychotic symptom profiles; however, women showed more anxiety and depression symptoms.

Limitations

- The detection methods were not assigned to the mental healthcare service at random.
- The two recruitment populations differed in age: screening was conducted in patients from age 18–35 years whereas the referred group was aged 14–35 years.
- Because the transition rate in the referred group was low, differences in diagnoses after psychosis onset could not be analyzed.

Introduction

Most psychotic disorders are preceded by a prodromal phase. This phase, prospectively called the 'at-risk mental state' (ARMS) phase, is a potential target for intervention to prevent or delay the onset of psychosis, or to improve the outcome by reducing the duration of untreated psychosis. It has been debated whether this ARMS phase should be added as an additional diagnosis in the DSM-V, called the attenuated psychosis syndrome (1). One of the counter arguments to the use of the ARMS is the declining transition rates to psychosis in ultra-high-risk (UHR) studies (2). In the earliest UHR studies, transition rates to psychosis were about 40% within 1 year (3, 4). Since then, UHR studies have reported declining transition rates of 7–16% within 2 years (5). Moreover, the proposed diagnosis has only been applied in research settings that attract ill individuals at rates disproportionate to those occurring in the overall population. It is unclear whether field tests away from these settings will result in the same conversion rates to psychosis. One of the main challenges in establishing the reliability and validity of ARMS is the recruitment of an adequate ARMS sample size, and limiting the number of false-positive cases (6).

Epidemiological studies in the general population have identified risk and environmental factors preceding the onset of psychotic disorders, that is, subclinical psychotic symptoms before the first episode (7, 8). However, screening methods in the general population revealed that these subclinical symptoms were highly prevalent and non-specific, so that an excess of false-positive individual cases were found to be at risk of psychosis (9–12).

Screening methods for detecting ARMS have been explored using a variety of populations. The first prospective early detection and intervention study was conducted by Falloon et al. (13), who trained general practitioners (GPs) in detecting early signs of schizophrenia. Later studies screened help-seeking persons in a primary care setting (14) or students in a general college population (15). However, high false-positive rates remained a problem.

Nowadays, ARMS is determined by a combination of risk factors, including genetic susceptibility as well as symptomatology (16). For example, the presence of two or more subclinical psychotic symptoms in a specific age group (14–35 years) of patients referred to a specialized clinic in combination with a depressed mood results in a 40% chance of developing a psychosis within 2 years (12). The reduction in false-positive cases reached by combining risk factors is accompanied by the disadvantage of finding more false-negative cases in the subsample that does not meet all the risk criteria.

The current case recruitment strategy of ARMS individuals in early-psychosis research relies on referral at suspicion of a psychotic development to a tertiary medical center, because performing the earlier screening methods in a general population resulted in too many false-positives. Studies using this method reported a mean annual recruitment of 18 ARMS cases per year per institute (17). For instance, McGlashan et al. (18) needed 4 years to recruit 60 ARMS patients by referral in a recruitment area with an expected yearly prodromal incidence rate of 600 persons. The prepsychotic symptoms are mostly subtle and not recognized as subclinical in the general mental health care (19); this could explain why many cases are missed when employing this strategy.

Sequential screening, first proposed by Bell (16), may offer a solution to both the false-positives and the missed cases. Sequential screening in detecting emerging psychosis involves the combination of a number of different risk factors (age, help seeking, social decline, genetic risk) and screening measures (interviews and questionnaires). A sample becomes more enriched with psychosis-prone subjects when it has passed through more mental health filters (10). That is why high proportions of people with psychosis or ARMS are found in those referred to tertiary specialized clinics. Most people who develop a psychotic disorder sought help in the secondary mental health services for non-psychotic mental disorders prior to the onset of psychosis (20). Screening in a consecutive help-seeking population may detect prodromal patients more efficiently. Therefore, the Dutch Early Detection and Intervention Evaluation (EDIE-NL) used a two-stage screening strategy in the complete help-seeking population (aged 18–35 years) in one site and the traditional referral method (aged 14–35 years) in another site (21). This offers the opportunity to explore differences between the screened and referred populations. A sample in a secondary mental health service has one filter less than a sample in a tertiary clinic, and we expect more false-positive cases using the Comprehensive Assessment of At-Risk Mental States (CAARMS) (3) in the less psychosis-prone secondary mental health service sample, even after prescreening with the Prodromal Questionnaire (PQ) (22).

Aims of the study

The present study examines similarities and differences in the ultra-high-risk population collected by screening, compared to the ultra-high-risk population collected by referral. We expect to find more false positives in the consecutive help-seeking population. We also expect to find more women with at-risk mental states, as more women seek help in the secondary mental health services (23).

Material and methods

This study analyzed data from the EDIE-NL study, which is a longitudinal randomized controlled trial comparing treatment as usual (TAU) with an add-on cognitive behavioral therapy (CBT) targeted at the prevention of psychosis. A comprehensive description of the study, aims, sample procedure, diagnostic instruments, randomization protocol, quality control procedures and analysis has been documented elsewhere (21).

The study was approved by the Dutch Union of Medical-Ethics Trial Committees for mental health organizations and was conducted in compliance with the Declaration of Helsinki (amendment of Edinburgh, 2000). The trial is registered at Current Controlled trials as trial number ISRCTN21353122.

Informed consent was given after the procedure had been fully explained. Informed consent was also obtained from parents or guardians if the participant was aged ≤ 18 years.

Setting and recruitment

The screening method was implemented in the secondary mental healthcare service PsyQ Haaglanden, which is the provider of secondary general adult mental health care for The Hague (±488 000 inhabitants) and Zoetermeer (±120 000 inhabitants). Help-seeking individuals, referred by their GPs or self-referred, were first interviewed by telephone and preselected for further assessment and diagnosis at a specific care program (e.g., anxiety disorders, depression, attention deficit hyperactivity disorder (ADHD), and six additional conditions). If people were aged 18–35 years old, they received the PQ (22)) by post. Participants were asked to fill in the questionnaire and to bring the PQ to the assessment and diagnosis appointment at the specific care program. If people scored positive on 18 or more of the 45 subclinical positive psychotic symptoms of the PQ, they were interviewed with the CAARMS (3).

Between February 2008 and February 2010, all 3671 consecutive help-seeking persons (in the age range 18–35) were prescreened with the PQ. Of these, 420 patients were interviewed with the CAARMS.

The referral recruitment method was practiced in the tertiary early-psychosis service of the Academic Medical Center in Amsterdam (±770 000 inhabitants). Patients were referred for a second opinion by psychiatrists, psychologists, GPs, outreach services, counseling services and schoolteachers, or the help seeking was initiated by the patient or their family. Between February 2008 and February 2010, 193 referrals in the age range 14–35 were assessed for an at-risk mental state of developing psychosis with the CAARMS. About 50% of these referrals originated from the city of Amsterdam; the remainder came from smaller towns and villages in the surrounding area.

Sample

The ARMS groups consists of three subgroups (3, 24): i) patients with a schizotypal personality disorder or a first-degree relative with psychosis; ii) patients experiencing attenuated positive symptoms, such as ideas of reference, odd beliefs, magical thinking or unusual perceptual experiences; and iii) patients who had experienced a brief psychotic episode of ≤1 week duration that resolved without antipsychotic medication (i.e., brief limited intermittent psychotic symptoms; BLIPS).

In addition, ARMS patients had to fulfill the criterion of impaired social functioning as assessed with the Social and Occupational Functional Assessment Scale (SOFAS (25), which means a SOFAS score of ≤55 and/or a drop in the SOFAS score of 30%.

Exclusion criteria were as follows: i) current or previous usage of a cumulative dose of antipsychotic medication of (in total) ≥ 15 mg haloperidol equivalent (e.g., maximum of 5 days of 3 mg); ii) severe learning impairment; iii) problems arising from an organic condition; iv) insufficient competence with the Dutch language; and v) history of psychosis.

Instruments

After signing informed consent, the baseline assessments were performed. Patients were then interviewed with the CAARMS after 2, 3, 6, 9, 12, 15, and 18 months. We report here on the 12-month results.

A comprehensive description of the instruments used in this study can be found elsewhere (21).

i) The Prodromal Questionnaire (22) (PQ; authorized Dutch translation by van der Gaag, Klaassen, and Wunderink and called the Experiences List) is a 92-item self-reporting questionnaire that assesses the presence of lifetime prodromal symptoms. Of these items, 45 refer to positive psychotic symptoms. A pilot study showed that a cutoff score of 18 resulted in a psychosis-prone enriched sample comprising about 15% of the help-seeking population.
ii) The Comprehensive Assessment of At-Risk Mental States (CAARMS) (3), including SOFAS (25), is a semi-structured interview conducted to determine the presence, severity, frequency, and type of ARMS symptoms. The EDIE-NL researchers received an extensive 2-day training from Dr. Alison Yung (one of the developers of the CAARMS). During the study period, reliability checks of the Dutch version of the CAARMS were performed about every 3 months. The pairwise interrater concordance of the CAARMS was 0.97 and was considered acceptable by the training team.
iii) Semantic verbal fluency is assessed with a subtest of the Groninger Intelligence Test. During a 60-second period, patients are asked to recall various animal names (26).
iv) Depression is assessed with the Dutch translation of the Beck Depression Inventory second edition (BDI-II-NL)(27).
v) The Calgary Depression Scale (CDS) is a 9-item interview that assesses depressive symptoms independent of the negative symptoms of schizophrenia (28).
vi) The Social Interaction Anxiety Scale (SIAS) is a 20-item self-report questionnaire measuring social anxiety (29).
vii) The Personal Beliefs about Illness Questionnaire-Revised (PBIQ-R) is a self-rating questionnaire that assesses the subjective appraisal of the illness (30).
viii) The Dutch version of the Schedules for Clinical Assessment in Neuropsychiatry (SCAN 2.1) was used to assess the DSM IV-diagnosis after transition to psychosis (31).
ix) The demographic questionnaire is a measure developed by the researchers to assess demographic characteristics, based on previous research and known risk factors for psychotic disorders.

Measurement of transition

The primary outcome measure is the transition to psychosis, as defined by the CAARMS criteria, or the start of using antipsychotic medication and a confirmation of the psychotic state by the CAARMS. After transition into psychosis, diagnoses were assessed with the SCAN 2.1 (31).

Statistical analyses

Group differences were explored using the Statistical Package for the Social Sciences (SPSS 18.0 Statistics, UK) for Windows. Comparison of baseline characteristics (age, level of education, sex, inclusion group, marital status, living situation, urban environment, bullying in the past and undesired pregnancy mother, school attendance, hand preference, ethnic identity, and drug use in the last year) between the screened sample and the referred sample was made with Pearson's two-tailed chi-square tests and independent sample *t*-tests.

Multivariate analyses of variance (MANOVA) were conducted to assess differences in baseline symptomatology, such as CAARMS symptoms, distress with positive symptoms, depressive mood, and anxiety.

Univariate analysis of variance (ANOVA) and chi-squares were performed on the 12-month follow-up transition rate.

Results

Demographic characteristics

The screening method found 52 psychotic patients and 147 patients at risk in a recruitment area of 608 000 people (prevalence ARMS: 0.024); 93 ARMS patients signed informed consent. In total, 193 patients were referred to the diagnostic center of the early-psychosis clinic in a recruitment area of at least 770 000 inhabitants; of these, 66 patients had full-blown psychotic symptoms, 66 subjects had an at-risk mental state (prevalence ARMS: 0.008), and 61 patients did not meet the ARMS or psychosis criteria; 40 ARMS patients signed informed consent. Most of those who did not sign informed consent were unwilling to do the additional testing during the study and/or to adhere to the additional intervention, apart from the disorder for which they originally sought help, or they dropped out of routine care.

A two-tailed independent samples *t*-test was performed to explore differences in age between the two populations in the study. People recruited by

Table 1. demographic characteristics for ARMS patients in screened and referred recruitment groups

	Screened		Referred				
	N = 93	Percent	*N* = 40	Percent	X^2	df	*P*
Sex							
Female	60	64.5	6	15.0	27.43	1	<0.0001
Inclusion group							
Genetic risk	16	17.2	7	17.1	0.49	3	0.92
Attenuated symptom	76	81.7	33	80.5			
BLIPS	1	1.1	0	0			
Marital status							
Married	34	36.6	2	5.0	20.48	2	<0.0001
Never married	51	54.8	38	95.0			
Divorced	8	8.6	0	0.0			
Living situation							
Living independently	15	16.5	7	17.5	36.90	5	<0.0001
With parents	24	25.8	30	75			
With partner and/or children	44	47.3	1	2.5			
Residential	1	1.1	0	0			
Other	7	7.5	2	5.0			
Missing	2	2.1	0	0			
Urban environment							
<10.000	0	0	3	7.5	100.9	4	<0.0001
10.00–100.000	13	14.0	14	35.0			
100.000–250.000	8	8.6	0	0.0			
250.000–500.000	72	77.4	0	0.0			
> 500.00	0	0.0	23	57.5			
Still in school							
Yes	20	21.7	15	38.5	3.91	1	0.048
Has a paid job							
Yes	51	56.0	14	35.9	11.13	6	0.084
Undesired pregnancy mother							
Yes	23	24.7	7	17.5	15.23	2	<0.0001
Breast feeding							
Yes	63	70.8	17	60.9	2.01	1	0.37
Bullied in past							
Yes	61	67.0	15	38.5	10.67	1	0.005
Hand preference							
Right handed	85	92.4	32	82.1	3.07	1	0.078
Ethnic minority							
Yes	52	55.9	19	47.5	0.80	1	0.372
Drug use last 12 months							
Yes	29	31.5	15	39.5	0.76	1	0.38

BLIPS, Brief limited intermittent psychotic symptoms.

screening were significantly older (mean = 25.5, SE = 0.51) than the referred subjects (mean = 20.6, SE = 0.68); (t (131) = 4.19, P = 0.043). No differences were found for mean years of education between the screened population (mean = 13.9, SE = 0.27) and the referred population (mean = 13.60, SE = 0.38); t (127) = 0.61, P = 0.55.

Table 1 presents data on the two-tailed Pearson's chi-square tests for several other demographic characteristics of the patients in both groups. The distribution of the subgroups within the ARMS group is remarkably similar in both recruitment strategies. There were significantly more women than men in the screened population. Most people in the screened population lived with their partner and/or children, whereas most patients in the referred population lived with their parents. Subjects in the screened population reported more bullying during their childhood, and their mothers more often reported that the pregnancy had been undesired. Most of the referred subjects were still studying. After correction for age and sex, significant differences remained for marital status (F (3, 129) = 18.02, P < 0.0001) and currently studying (F (3, 129) = 4.97, P < 0.0001).

Psychopathology

After meeting the criteria for the assumptions of parametric tests, two-tailed multivariate Analysis of Covariance (MANCOVA) was performed to explore the differences in psychopathology between the screened and the referred population (Table 2). The analysis was corrected for age, sex, and the interaction effect site*sex, because the age and gender profile differed significantly between both

Table 2 Psychopathology (corrected for age, sex, and site*sex) for both recruitment ARMS groups using MANCOVA

	Screened $N = 93$ Estimated mean (SE)	Referred $N = 40$ Estimated mean (SE)	F	df	P
SOFAS	46.83 (0.560)	45.69 (1.24)	0.673	1	0.414
Depression BDI	28.78 (1.15)	15.71 (2.53)	14.56	1	<0.0001
Calgary depression scale	7.16 (0.48)	3.37 (1.07)	10.03	1	0.002
Sias	35.88 (1.74)	24.11 (3.84)	7.48	1	0.007
PBIQ	77.51 (1.52)	68.80 (3.37)	5.33	1	0.023
MANSA	49.15 (1.31)	55.89 (2.91)	4.28	1	0.041
Word fluency	20.94 (0.64)	21.41 (1.40)	0.087	1	0.77
CAARMS					
Total positive symptoms	10.73 (0.31)	9.85 (0.69)	1.284	1	0.26
Total distress	192.33 (8.13)	146.69 (17.97)	5.14	1	0.025
Total cognitive changes	3.33 (0.18)	3.36 (0.40)	0.004	1	0.95
Total emotional disturbance	4.02 (0.24)	3.49 (0.54)	0.77	1	0.38
Total negative symptoms	7.96 (0.31)	6.73 (0.68)	2.59	1	0.11
Total behavioral changes	9.84 (0.35)	8.49 (0.78)	2.40	1	0.12
Total motor changes	4.82 (0.34)	3.41 (0.74)	2.89	1	0.092
Total general psychopathology	16.58 (0.55)	13.85 (1.22)	3.95	1	0.049

SOFAS, Social and occupational functioning assessment scale; BDI, Beck depression inventory; CDS, Calgary depression scale; SIAS, social interactions anxiety scale; PBIQ, personal beliefs about illness questionnaire; MANSA, Manchester short assessment of quality of life; CAARMS, comprehensive assessment of at-risk mental states.

groups. The screened population scored significantly higher than the referred population on the Beck Depression Inventory scale, the Calgary depression scale, the Social Interaction Anxiety Scale, the Personal Beliefs about Illness Questionnaire, and on distress (CAARMS) and total general psychopathology (CAARMS). MANCOVA showed that these differences were significantly influenced by site (F (7) = 2.68, P = 0.013) and age (F (7) = 4.58, $P < 0.0001$), but not by sex (F (7) = 0.282, P = 0.96) or the interaction site*sex (F (7) = 0.73, P = 0.643).

Transition to psychosis

A transition is defined by the CAARMS criteria or the start of using antipsychotic medication and a confirmation of the psychotic state by the CAARMS. At 12 months, 78 patients were in the screening condition (attrition 16%) and 32 in the referred condition (attrition 20%). In the screened population, 21 ARMS patients made the transition to psychosis vs. 3 ARMS patients in the referred population. This difference is significant ($X^2(1, n = 110) = 4.1$, $P = 0.043$. There were no differences in the transition rates between the sexes. It was not possible to explore differences in transition diagnoses, as the transition rate in the referred population was too low.

Discussion

The current study is the first to explore the differences in samples of patients at ultra-high risk of developing psychosis recruited by screening in a secondary mental health service compared to a sample that was referred to the diagnostic center of a tertiary specialized clinic for early psychosis. The results are not conclusive, but are necessarily preliminary as the institutes were not randomly assigned to one of the recruitment conditions.

The results show at least a three-fold higher proportion per capita of at-risk mental states in the screened population compared to the referred group. As in this calculation, we only included the number of inhabitants of Amsterdam city and excluded the number of inhabitants of the surrounding towns/villages; the ratio is in fact even more in favor of screening. Compared with the referred sample, the screened patients differed on demographic characteristics and psychopathology. On average, the screened sample was older, more often female, more often married and employed. In terms of psychopathology, the screened population showed more symptoms, such as depression, anxiety, and more distress from their subclinical positive psychotic symptoms. On the other hand, they did not report more subclinical psychotic symptoms. Comparison between the referred population and referred populations in previous ARMS studies reveals a similar proportion of detected ARMS patients per institute, that is, 18 patients per institute per year (17). The predominantly young male population in the referral condition is also similar.

At 12-month follow-up, the screened population showed more transitions to psychosis than the referred population (22.5% vs. 7.5%, respectively). The low rate in the referred population was also reported in other studies (5). This might be due to

the additional risk factor 'help-seeking for mental problems' in the screened population (12). For instance, a higher rate for depression is associated with the late prodromal stage of psychosis, which is in line with the higher depression scores for the screened population (32, 33). We believe that the arguments for the decline of transition rates in referral samples owing to better awareness are not applicable to the screened population (2).

These findings, in particular the higher proportion of the at-risk mental state and the higher transition rate in the screened population, suggest that screening a help-seeking population entering the secondary mental health services for non-psychotic problems detects patients who are in a late prodromal stage. Community health caretakers do not routinely assess subclinical psychotic symptoms. As a result, many of these patients might have been overlooked using the traditional referral process to the specialized clinical research settings. This is supported by the detection of 52 psychotic patients in the screened population, who were not diagnosed as such. In addition, the referral group showed 66 subjects already suffering from a psychosis while they were referred for at-risk mental states. The latter result is in line with previous studies reporting a seven times longer duration of untreated psychosis in patients who were treated in the secondary mental health care for non-psychotic disorders (34, 35) and in patients visiting GPs for psychological problems (19).

The screened population included more women, in contrast to referral studies on the early detection of high-risk groups. This is not surprising, as women seek help more often for other psychiatric problems (20, 23), and two-third of the complete screened help-seeking population was female. In the model of Van Os et al. (8), women with a psychosis started more often with positive and affective symptoms, social conflict and help-seeking behavior compared to men who suffer more from cognitive and negative symptoms and tend to socially withdraw.

The observed predominance of women may also be explained by the scope of the detection methods. On the one hand, the screening strategy was successful in covering a broader range of psychoses, namely where psychotic symptoms and affective symptoms overlap. The screening method included mood disorders with psychotic features and bipolar disorders, which are also associated with women (36, 37). On the other hand, subjects in the referred sample were mostly referred based on suspicion for developing a schizophrenic psychosis. Therefore, it is expected that the referred group will show more negative symptoms as well as social decline compared to the screened sample. Contrary to our expectations, both groups showed comparable levels of negative symptoms.

Detection of the large percentage of women raises the question as to whether screening detects a different (older female) group of high-risk patients. However, the results show that the differences in subclinical positive and negative symptoms, as well as psychopathology, in the ARMS stage were generated by site and age; no effect was found for sex. Thus, it appears that both men and women reported the same degree of subclinical psychotic symptoms. This is in line with previous research, which suggests that females fell ill 3–4 years later, but that sex had no substantial impact on the core symptoms of schizophrenia (38). Nonetheless, Lewine found differences in the premorbid functioning in men and women (39). However, it is not clear whether these differences are the result of age and sex being confounders. Schizophrenia might be the same disorder in the two sexes, but has an early onset in men and is thus associated with typical schizophrenic symptoms and poor premorbid functioning.

In the present study, the difference in age between the two locations is partly the result of the selected age range of the recruitment population. The tertiary psychosis clinic recruits patients aged 14 years and older, whereas the screening was implemented in PsyQ Haaglanden, which provides care for adults only (aged $\geq$ 18 years). The mean age for having an at-risk mental state, and the mean age at psychosis onset, varies between studies conducted in different populations. Recruitment in an adolescent population results in the finding of a young ARMS cohort, with a mean age of 19 years (40, 41). Clinical trials in adult cohorts reported an average age of 25 years (42) and 26 years (43). Häfner et al. even found a mean psychosis onset age of 29 years (38). This supports our suggestion that referral and research on high-risk patients and first-episode patients is biased toward young patients.

Clinical implications

Patient recruitment of the current early-psychosis studies depends on signaling a psychotic or schizophrenic development by referrers. However, the screening method in the present study detected more patients with an at-risk mental state of developing psychosis. This suggests that many psychotic developments are missed by untrained community health caretakers, who are the most important referrers to the specialized clinical research centers. Screening will most probably

lead to the early detection of females and older patients who are often overlooked because of a bias favoring young males in detecting psychosis. The screened sample had a higher transition rate than the referred sample; this strongly suggests that screening did not lead to more false-positive cases.

The screening method detects more patients at the gate of the mental health services and prevents under-diagnosis and under-treatment. In our opinion, screening does not provide an avenue toward the early detection of the genetic group (one of the three groups described as being at risk), as they do not necessarily have subclinical psychotic symptoms. Neither does it lead to an early detection of patients who have been in care for a longer period before the onset of psychotic symptoms, as the screening is only conducted at initial assessment. Nevertheless, we believe that screening, as well as referral options, should play a more prominent part in the general secondary mental health care.

Despite the advantages of the screening method, some disadvantages also exist. The most important concerns the greater amount of staff time required as a result of a lower specificity compared to a referral strategy. Of the 420 PQ positives, 52 (12%) were diagnosed as being psychotic and 147 (35%) were diagnosed with ARMS with the CAARMS. This means a total PQ true-positive rate of 47% and a false-positive rate of 53%. Similarly, the 193 referred patients yielded a total true-positive rate of 68% and a false-positive rate of 32%. As a result, the screening method required more interview time. The burden on the patient is that they had to complete the PQ and a CAARMS interview taking (on average) about 1 h.

In addition, the higher false-positive rate could lead to stigmatizing patients who were, with hindsight, not at ultra-high risk of developing psychosis. However, to prevent stigma in people with ARMS, they were informed that the criteria were for a risk profile to develop future psychiatric problems (without mentioning psychosis) and that it might be possible to prevent these future problems with an add-on intervention. Offering help was not stigmatizing, as these people were in fact seeking help from the start.

Strengths and limitations

The study has several strengths and limitations.

The main limitation is that, because this is an explorative study, the two recruitment strategies were not assigned at random to the sites; therefore, the results should be interpreted with caution. A randomized controlled trial testing the detection methods will provide a more comprehensive test of the potential contribution of screening in secondary mental healthcare services in the early detection of psychosis.

A second limitation is the small sample size of the referred population. Nevertheless, the characteristics of the referred sample are in line with other tertiary specialized early-psychosis departments.

A third limitation is the use of the self-report questionnaires, such as the Beck Depression Inventory and the Social Interaction Anxiety Scale. This may distort the findings by introducing report biases, such as over- or under-reporting of symptoms. Again, caution is therefore required in interpreting the outcomes. On the other hand, we emphasize that the Calgary Depression Scale and the CAARMS interviews that were conducted by trained psychologists show the same results as the self-report questionnaires. This indicates that the subjects made a reliable report of their symptoms on the self-report questionnaires.

A fourth limitation concerns the study populations. The screening method was conducted in patients aged 18–35 years, whereas the age group of the referred group was 14–35 years. This might explain the differences in mean age, marital status, and living situation, apart from the sex differences. The screening method missed the UHR adolescents, as PsyQ Haaglanden only provides care for patients aged ≥ 18 years. Therefore, it is not possible to explore and compare the exact prevalence of help-seeking patients at risk of psychosis. However, if the age range of the screened population was as large as for the referred population (14–35 years), the numbers may have given an even clearer indication in favor of the screening method, as the screening would also detect the UHR adolescents in addition to the UHR adults.

A fifth limitation is that the patients were followed up for only 12 months; patients in the earlier prodromal stage in the referred condition probably had such a low transition rate because they need more time to develop frank psychosis. The lower transition rate in the referred group might be the result of the detection of an at-risk mental state in a much earlier stage than detected by screening. A follow-up period longer than 1 year is required to test this hypothesis.

The final limitation is that the transition rates are possibly affected by the treatment offered to a part of the ARMS group. Subjects in both the referred and the screened population were randomly assigned to a treatment-as-usual group and to a group receiving a treatment-as-usual with an add-on cognitive behavioral therapy targeting the high-risk symptoms. Thus, transition rates might be lower than those in naturalistic studies, as the

intervention aimed to reduce the number of transitions to a first-episode psychosis. Second, the transition rate in the referred group was low; this resulted in a deficiency in analyzing differences in psychotic onset diagnoses between the two recruitment strategies.

A major strength of this study is the fact that the screened population consisted of a representative sample of all consecutively help-seeking patients in a well-described region, and that this sample was compared to a referred population.

A further strength is that the study has strong internal and external validity. The early detection of psychosis was implemented in routine care in both services. This has an immediate and positive effect on clinical practice. All raters who interviewed the patients in the different institutes were trained by Dr. A Yung and were given fidelity checks every 3 months.

We conclude that screening for psychotic symptoms in a help-seeking population aged 18–35 years leads to detection of an ARMS group that is comparable on subclinical psychotic symptoms to the ARMS group in a referred population. The higher transition rate, higher age, and the higher levels of depression, anxiety, and distress in the screened group might indicate a later prodromal stage in the ARMS group than when people are at-risk and are referred to a tertiary specialized clinic. The larger proportion of female ARMS patients in the screening recruitment strategy might reflect the fact that, compared to men, women more often seek help in secondary mental health care.

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